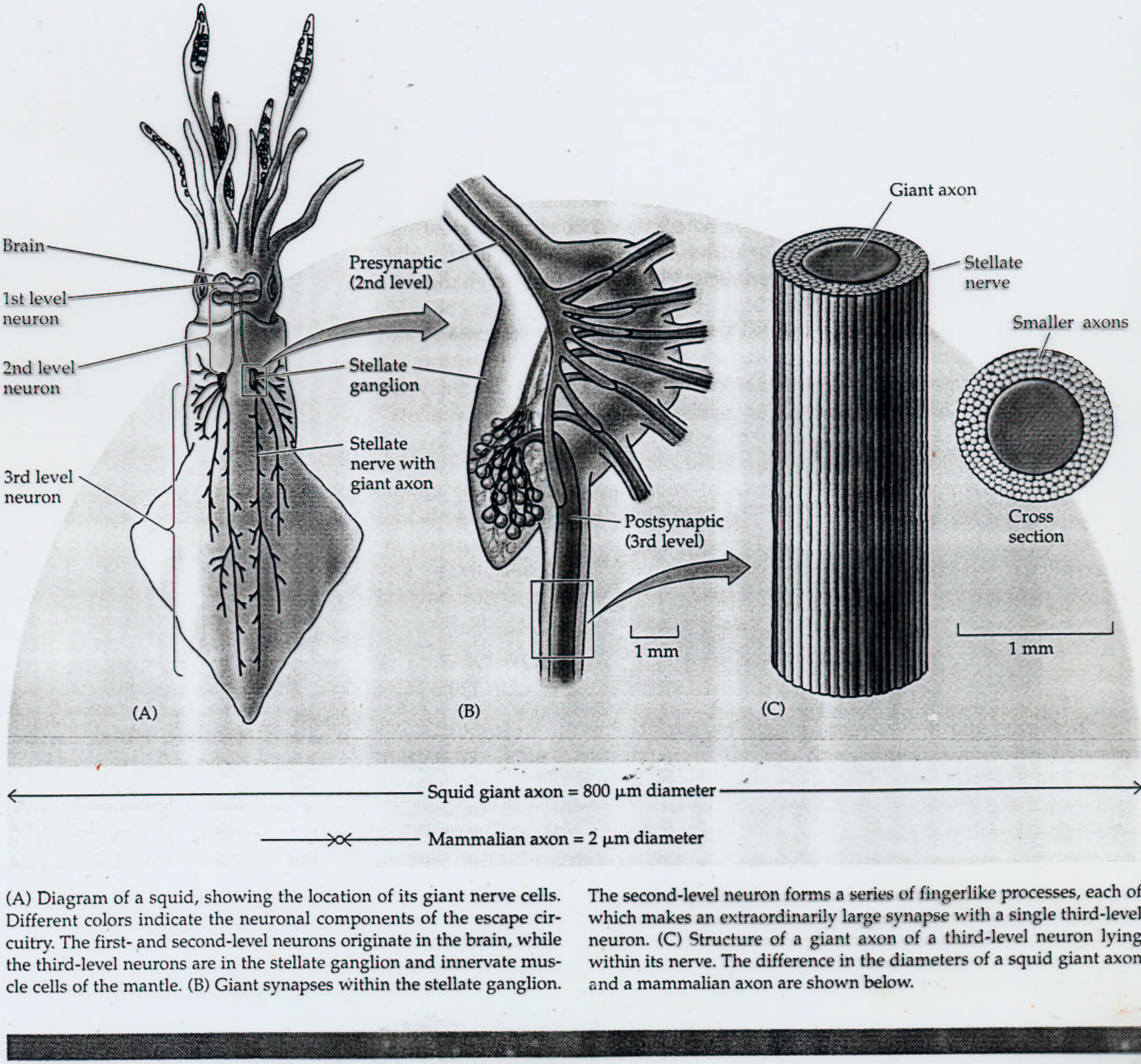
Box A
THE REMARKABLE GIANT NERVE CELLS OF SQUID

Many of the initial insights into how ion concentration gradients and changes in membrane permeability produce electrical signals came from experiments performed on the extraordinarily large nerve cells of the squid. The axons of these nerve cells can be up to 1 mm in diameter—100 to 1000 times larger than mammalian axons. Squid axons are large enough to allow experiments that would be impossible on most other nerve cells. For example, it is not difficult to insert simple wire electrodes inside these giant axons and make reliable electrical measurements. The relative ease of this approach yielded the first intracellular recordings of action potentials from nerve cells and, as will be discussed in the next chapter, the first experimental measurements of the ionic currents that produce action potentials.



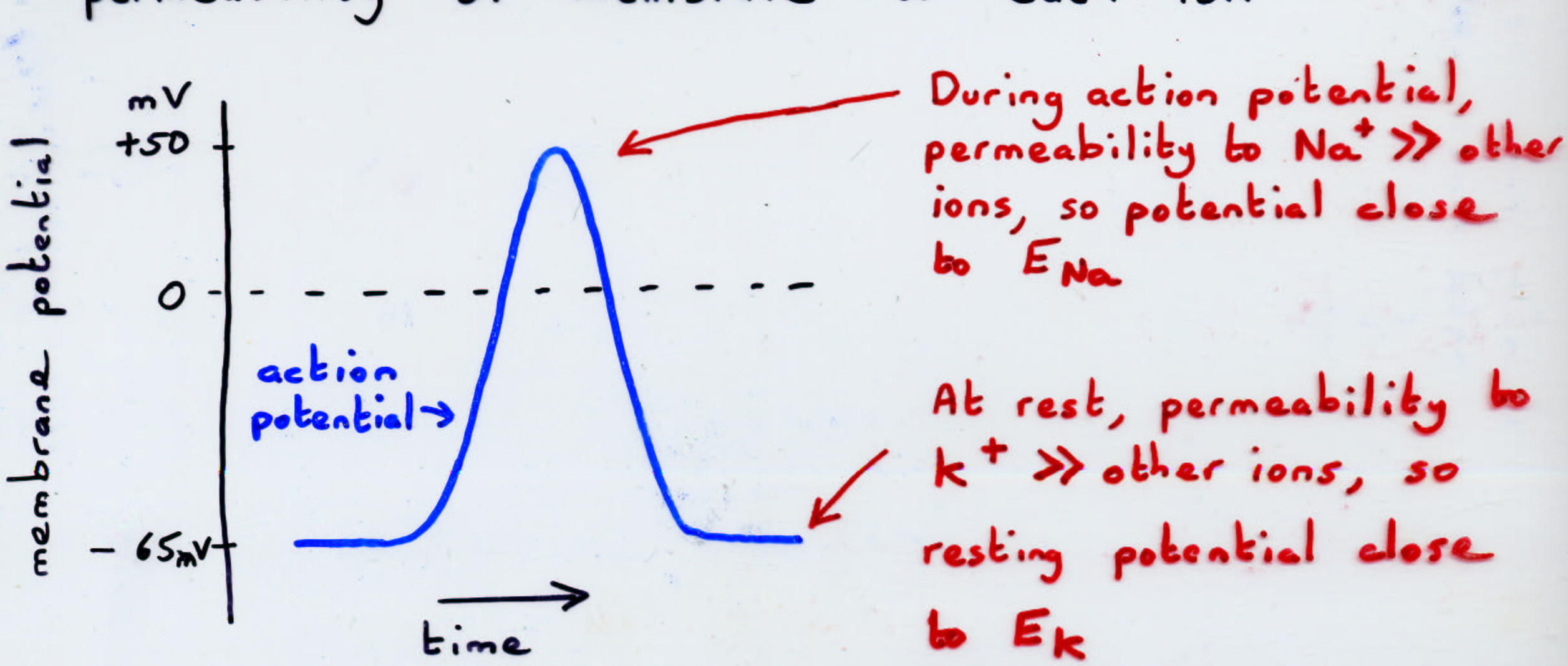
(A) Diagram of a squid, showing the location of its giant nerve cells. Different colors indicate the neuronal components of the escape circuitry. The first- and second-level neurons originate in the brain, while the third-level neurons are in the stellate ganglion and innervate muscle cells of the mantle. (B) Giant synapses within the stellate ganglion. The second-level neuron forms a series of fingerlike processes, each of which makes an extraordinarily large synapse with a single third-level neuron. (C) Structure of a giant axon of a third-level neuron lying within its nerve. The difference in the diameters of a squid giant axon and a mammalian axon are shown below.

Electrochemical Equilibrium in a multi-ion environment (i.e. what about real cells?)

for squid axon (resting potential = -65mV)

Ion	[out] mM	[in] mM	Nernst Potential (E) mV inside relative to outside
K^+	20	400	-75
Na^+	440	50	+55
Cl^-	560	~100	-43
Ca^{2+}	10	0.0001	+145

Actual potential depends upon relative permeability of membrane to each ion



Voltage across a membrane permeable to multiple ions given by Goldman equation

$$V = 58 \log \frac{P_K[K]_{out} + P_{Na}[Na]_{out} + P_{Cl}[Cl]_{in}}{P_K[K]_{in} + P_{Na}[Na]_{in} + P_{Cl}[Cl]_{out}}$$

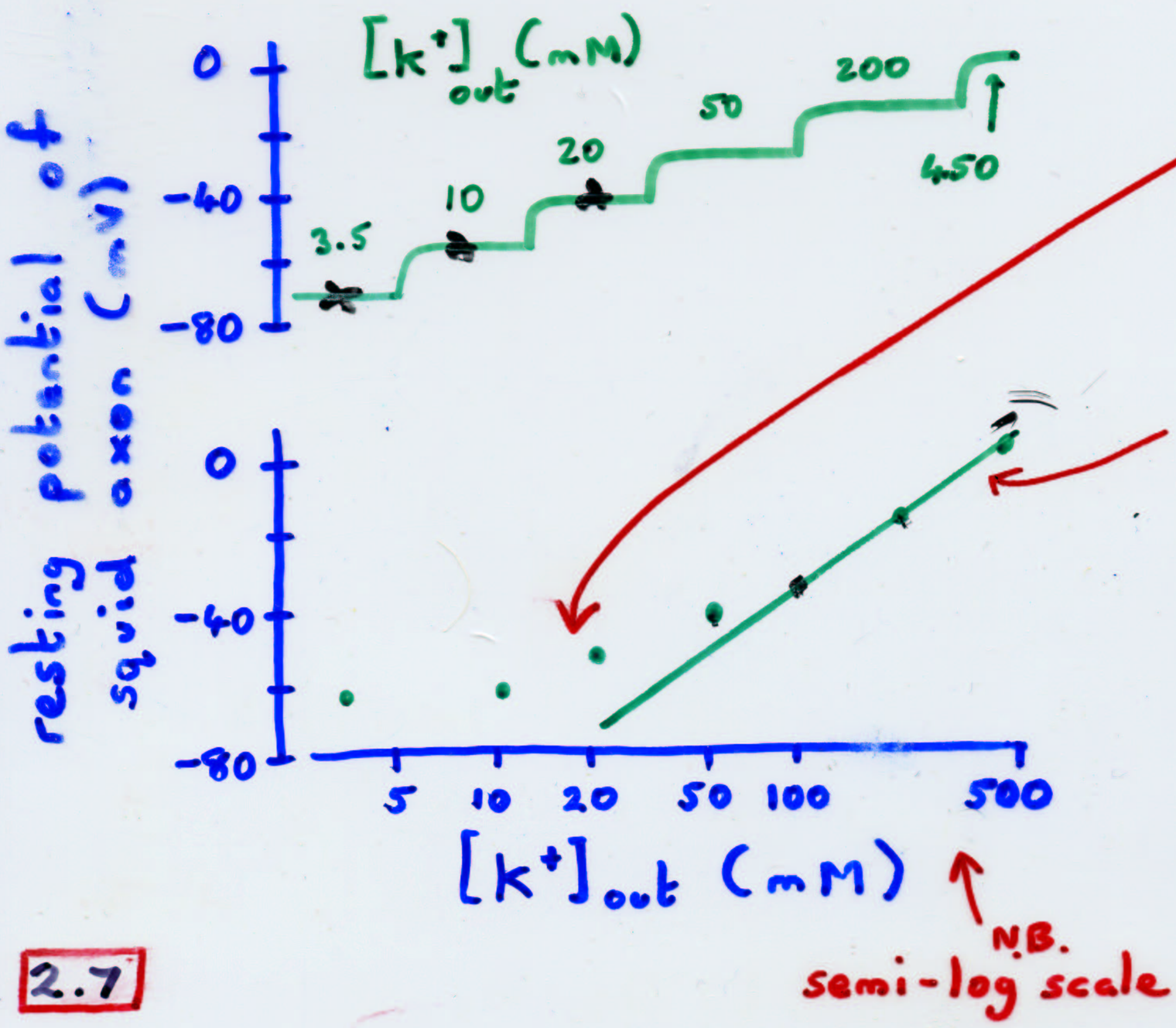
V: voltage in mV

P_K, P_{Na}: permeability to K^+, Na^+ etc.

$[Na]_{out}$, $[Na]_{in}$: extracellular / intracellular concentrations

$[Cl]_{in}$: note Cl is negatively charged

Experimental evidence that resting potential set by K^+ concentration gradient

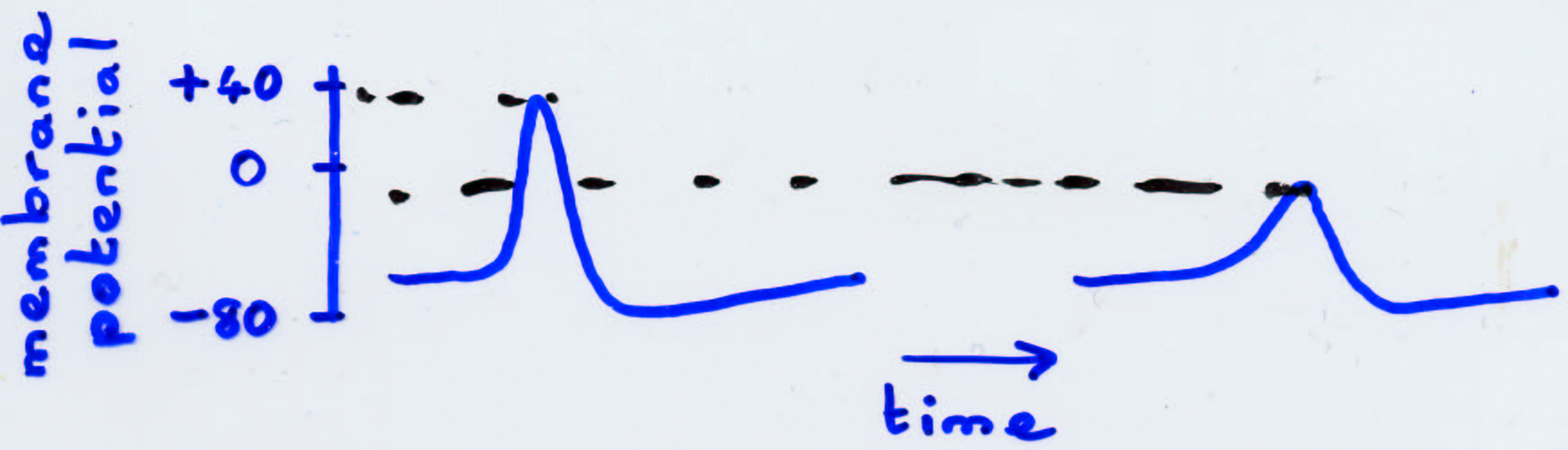


shallow slope as permeability to other ions becomes significant

slope = 58 mV / tenfold change in K^+ concentration gradient. (i.e. Nernst relation)

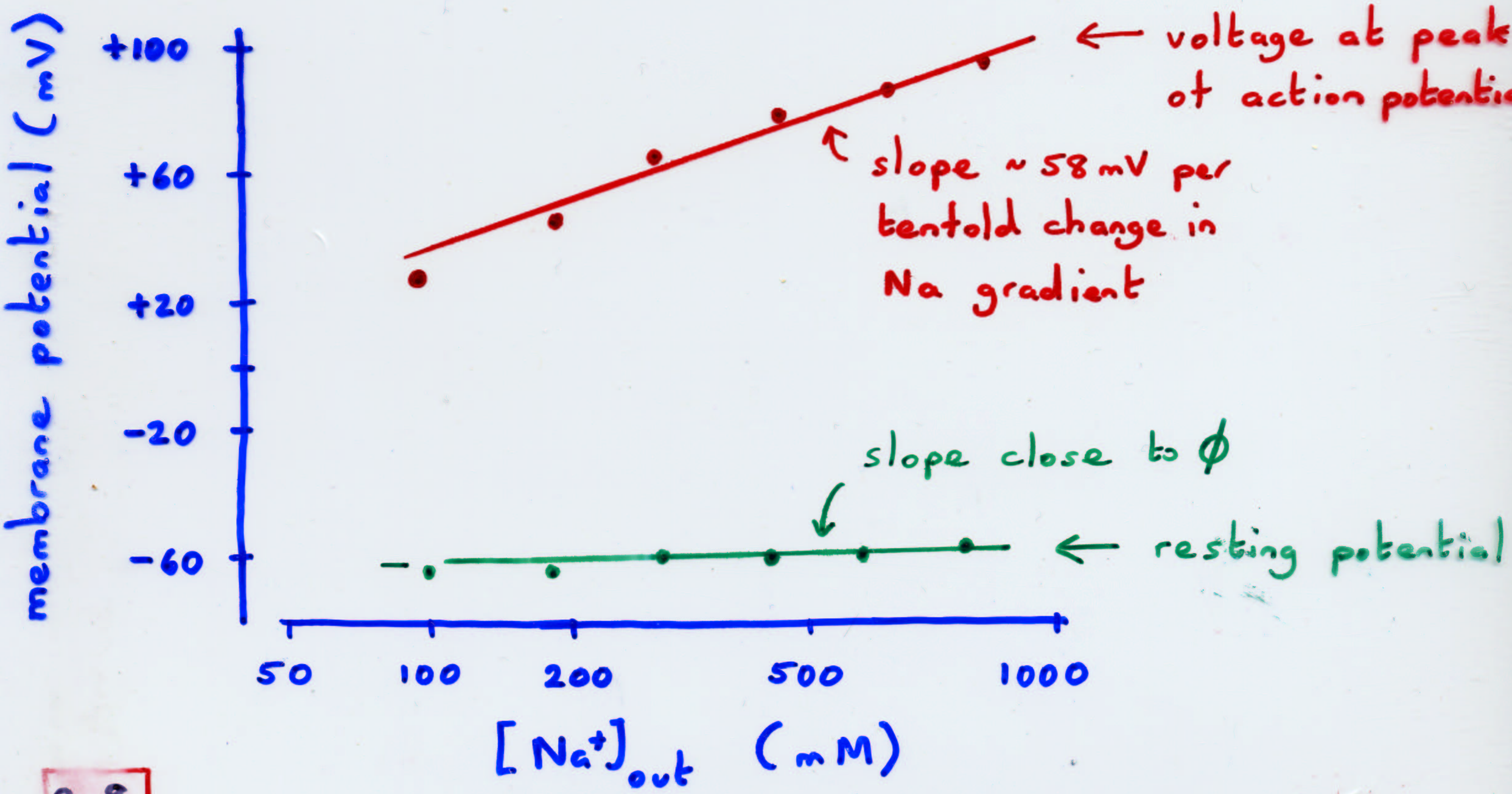
Ionic basis of the action potential

Peak height of action potential depends on $[Na^+]_{out}$



Normal extracellular $[Na^+]$

Low extracellular $[Na^+]$



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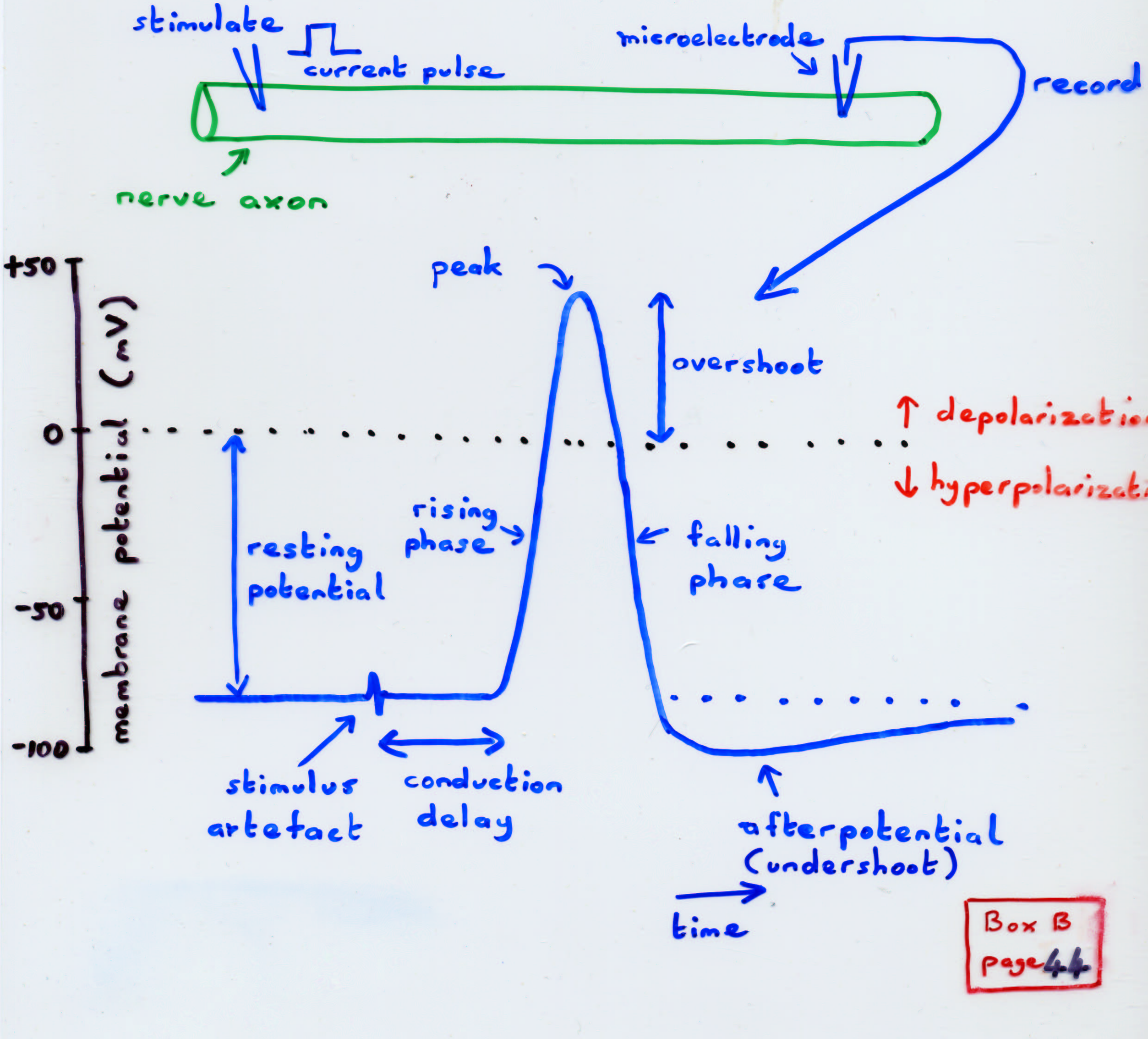
The Action Potential

A regenerative depolarization that propagates actively along a nerve or muscle cell.



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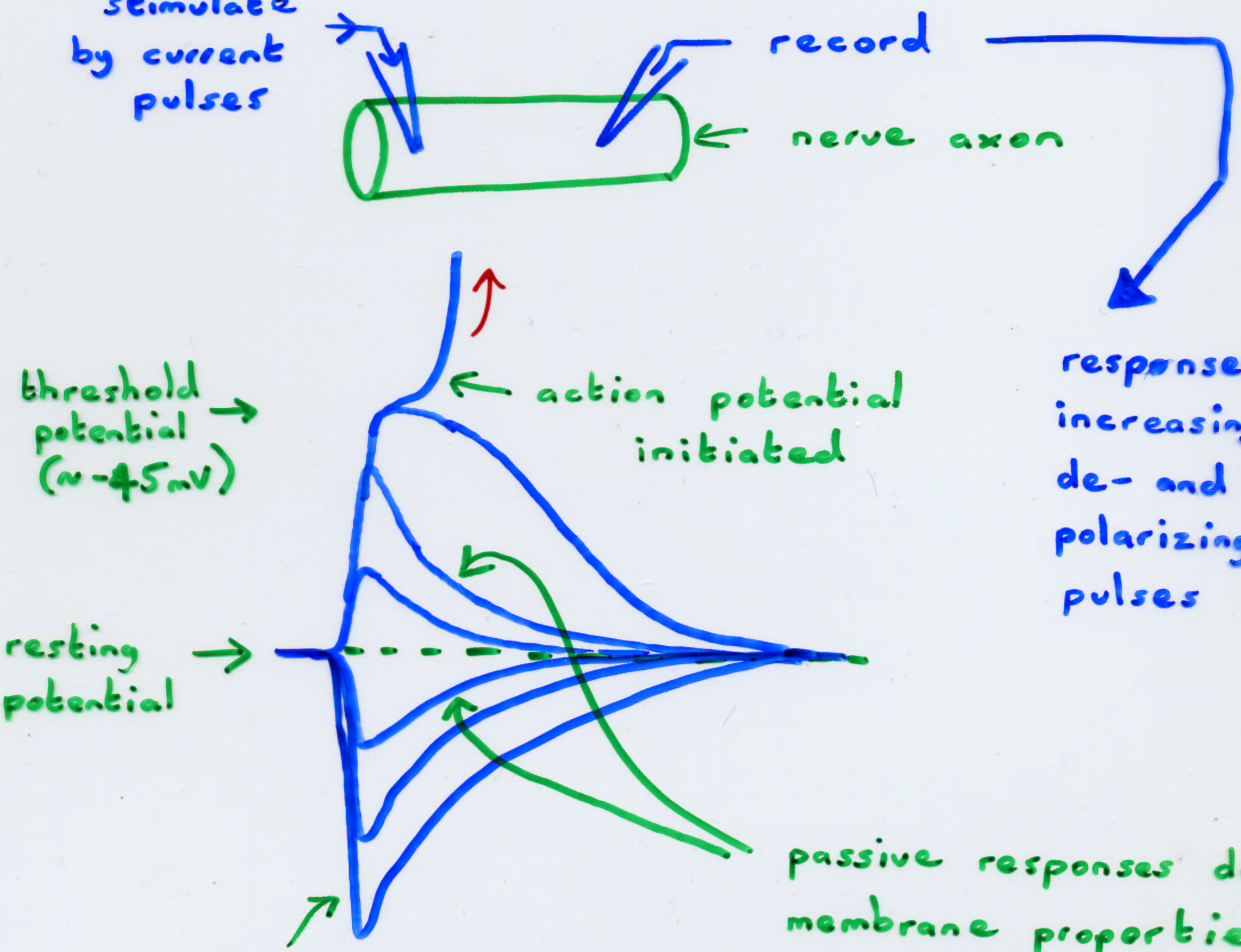
Characteristics of the action potential

① A threshold level of depolarization is needed to trigger an action potential.



② Action potentials are all-or-none events.

Once stimulus exceeds threshold, size of action potential is independent of stimulus strength (like flushing a toilet!)

③ Action potentials propagate without decrement at a finite speed.

As action potential travels along an axon it stays the same size. Speed is fast by biological standards (several $m\ s^{-1}$) but much slower (a million times) than electrical signal through a wire.

④ Refractory period.

After one action potential there is a short time (~a few ms) when an axon cannot be stimulated to give another.

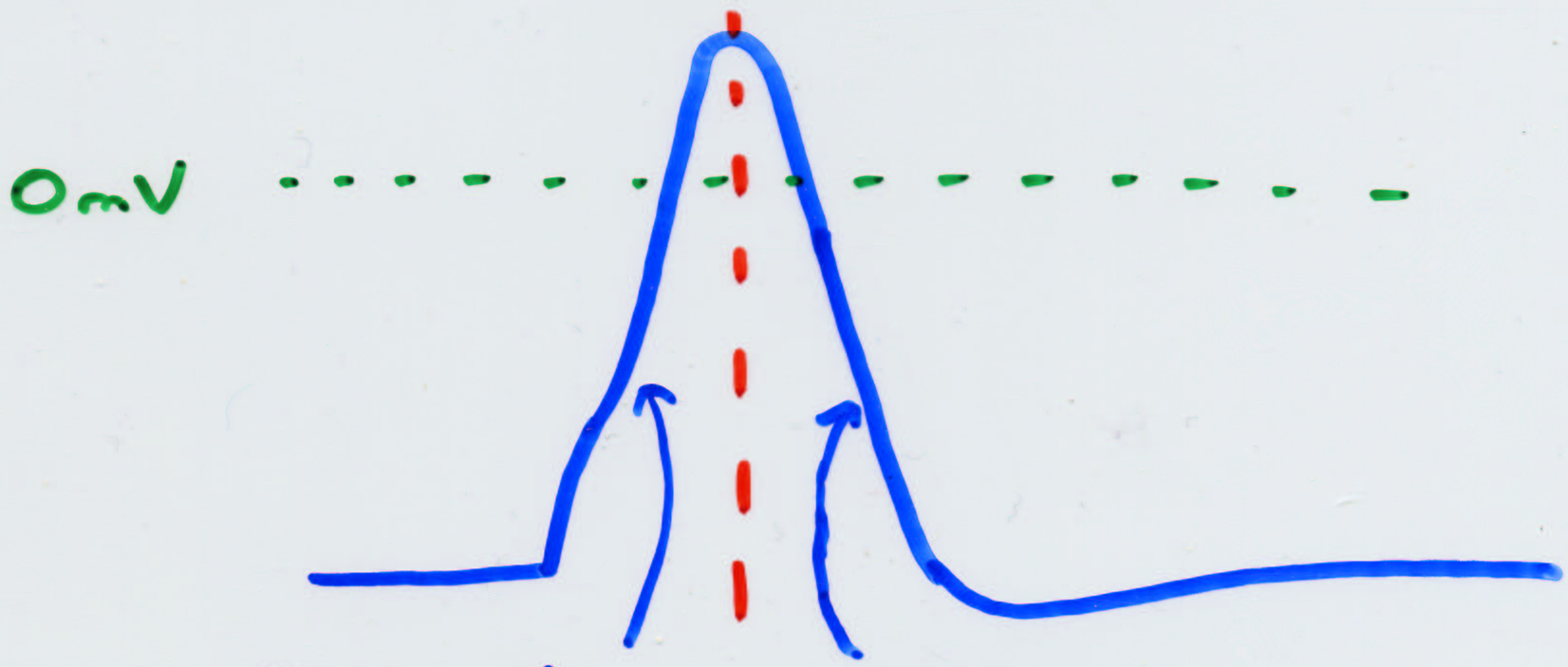
Important because:

(i) It stops action potentials going 'backwards'

(ii) It sets a limit to the maximum frequency of action potentials a nerve can transmit

Qualitative explanation of the Action Potential

Action potential is brief time when membrane potential is 'flipped' – positive rather than negative inside. This arises because cell membrane briefly becomes highly permeable to Na^+ ions, which rush into cell down concentration gradient and depolarize it.



regenerative process

① Depolarization opens voltage-sensitive Na^+ channels.

② Na^+ enters cell causing;

③ Cell depolarization

① Na^+ channels inactivate, so no more depolarizing current

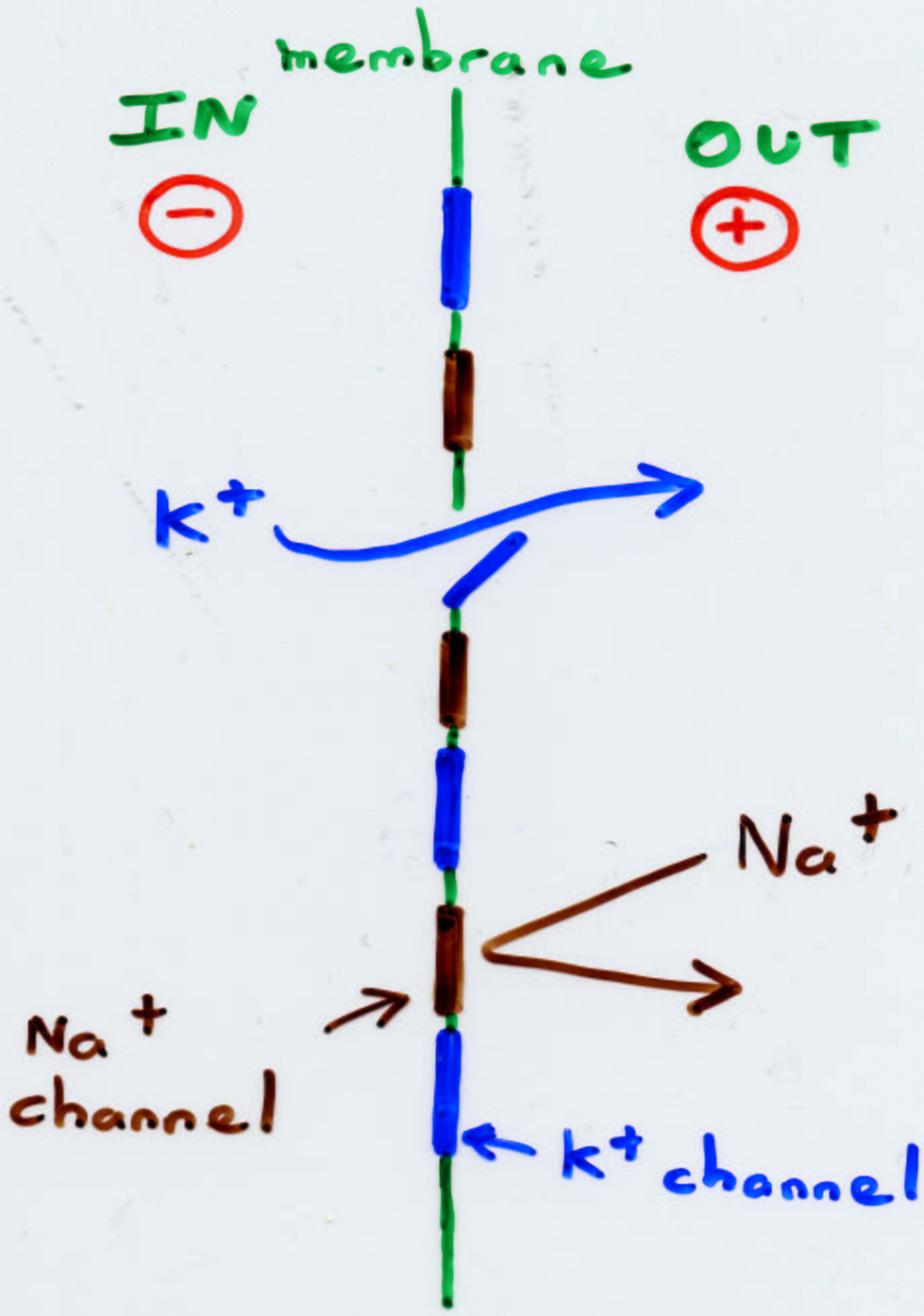
② Extra k^+ channels slowly open in response to depolarization.

③ Efflux of k^+ ions from cell hyperpolarizes it back toward the k^+ equilibrium potential.

Ion movements and permeabilities during the action potential

equilibrium potentials $E_K = -80mV$ $E_{Na} = +60mV$

At rest

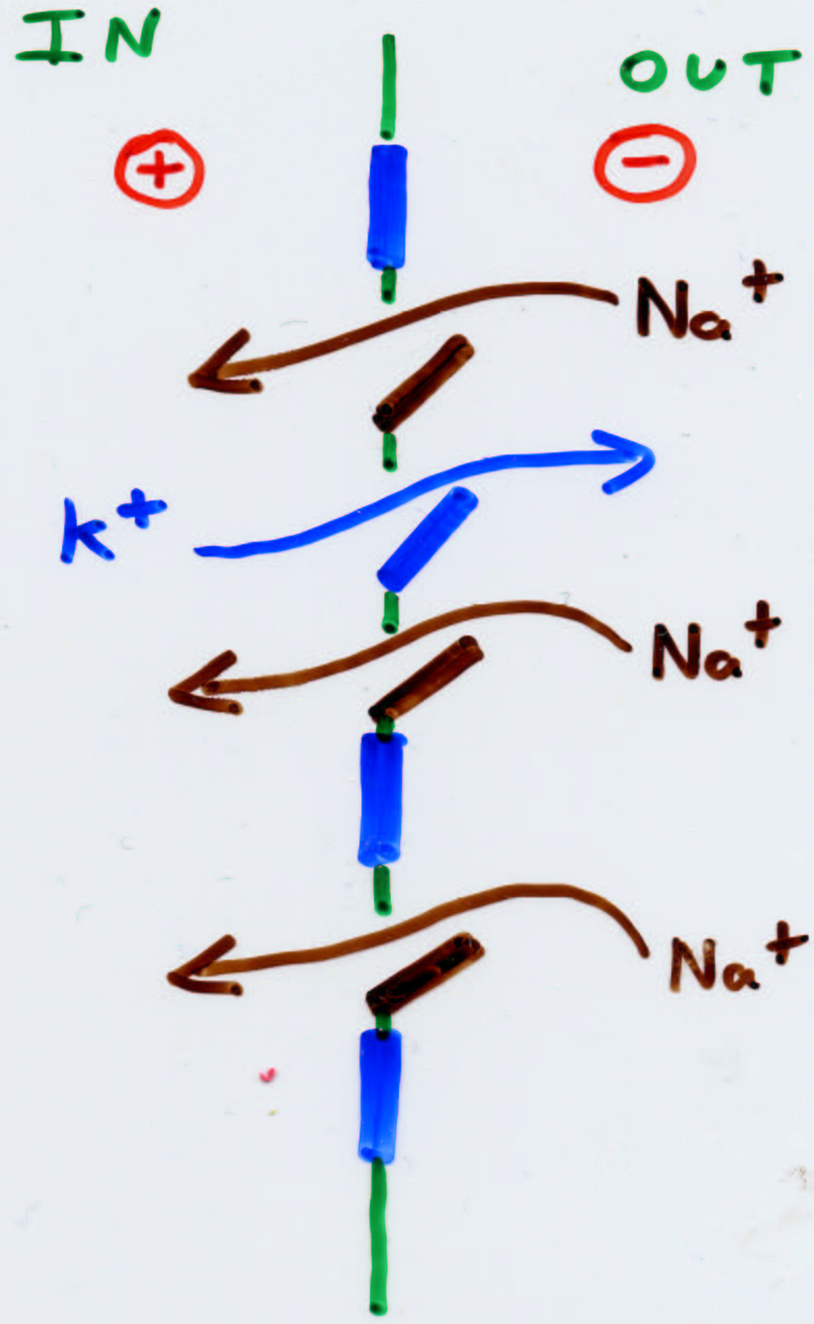


small resting permeability to k^+

virtually no permeability to Na^+

so resting potential close to $E_K = -80mV$

Rising phase of action potential

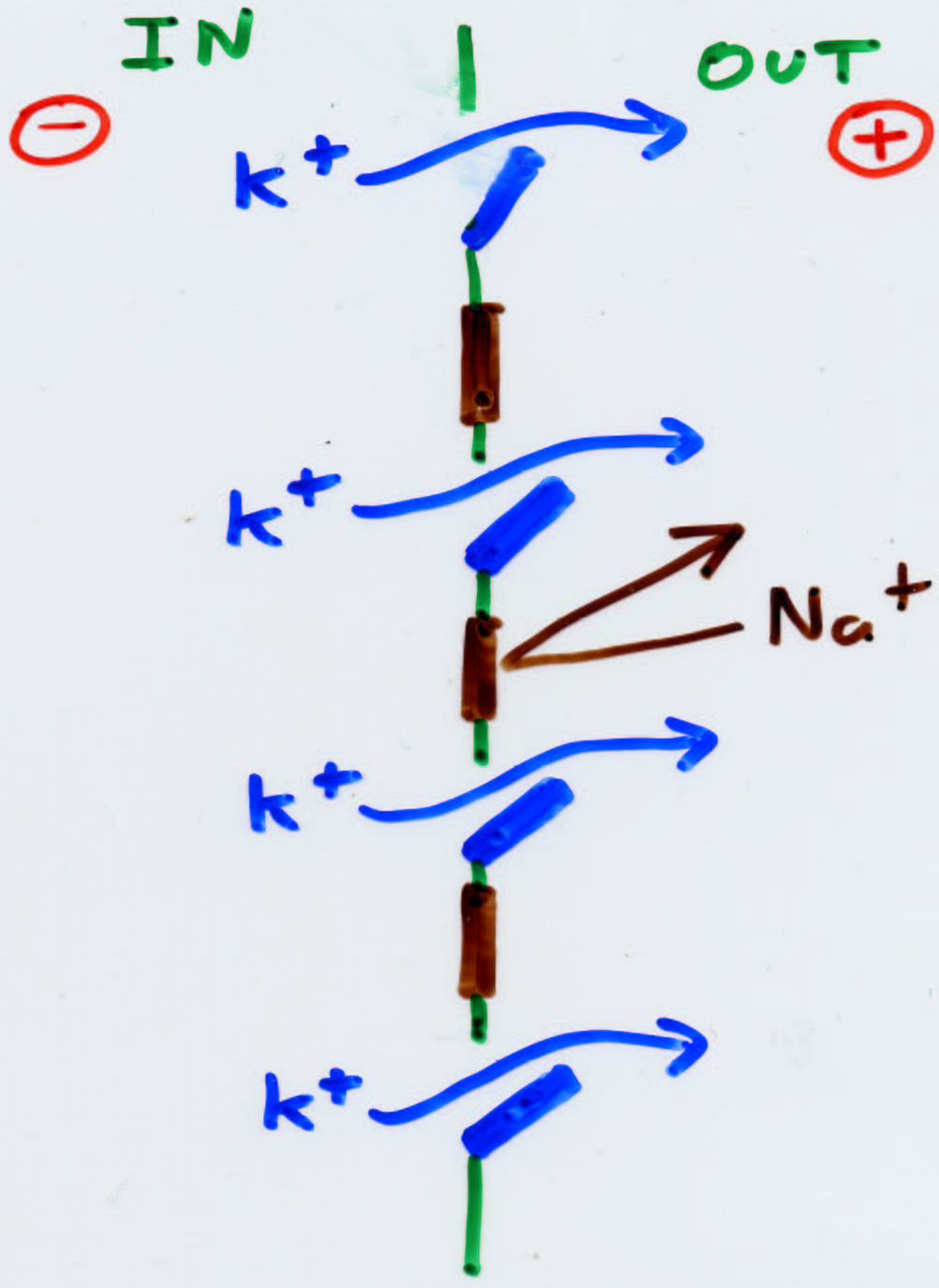


Na^+ channels are voltage dependent — open in response to depolarization.

→ Na^+ influx causes more depolarization, so more Na^+ channels open, so more Na^+ influx ....etc

Since Na^+ permeability now $\gg$ k^+ permeability potential at peak of action potential close to E_{Na}

Falling phase of action potential



Na^+ channels inactivate (spontaneously close) within about 1ms

k^+ channels are voltage dependent — open with depolarization, but slowly.

k^+ permeability is now $\gg$ Na^+ permeability so potential quickly returns toward E_k = -80mV

How much Na^+ enters an axon during an action potential?

Very little — only enough to charge the membrane capacitance from −80 mV to +60 mV.

Intracellular $[Na^+]$ rises $\ll 1\%$ during a single action potential.

Even if Na^+ pump poisoned, an axon will transmit > 1000 action potentials